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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/764,390	01/23/2004	Arthur B. Raitano	511582008100	2022

25225 7590 01/09/2008

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EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
01/09/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/764,390	RAITANO ET AL.	
	Examiner	Art Unit	
	Karen A. Canella	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *49,54,56-58,63,66,72,75,79 and 80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *49, 54, 56-58, 63, 66, 72, 75, 79 and 80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 49, 54, 56-58, 63, 66, 72, 75 and 79-80 are pending and under consideration.

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 49, 54, 56-58, 63, 66, 72, 75, 79 and 80 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility.

Claims 49 and 57 are drawn to an isolated or recombinant polypeptide comprising SEQ ID NO:3, 5 or 7, and composition thereof. Claims 75 and 77 are drawn to a method of detecting cancer in a patient comprising determining the expression level of a polypeptide comprising SEQ ID NO:3, 5 or 7. Claims 54 and 56 are drawn to a polypeptide consisting of nine, ten or fifteen contiguous amino acids of SEQ ID NO:3, 5 or 7 wherein the peptide induces a specific antibody response against a polypeptide having SEQ ID NO:3, 5 or 7. The specification asserts that 254P1D6B can be used in the same manner as other tumor antigens such as PSA, because 254P1D6B is expressed in lung, ovary, prostate, pancreas and breast tissues, when said tissues are malignant (page 122). The specification sets forth the polynucleotide of 254P1D6B v.1 clone LCP-3 as encoding SEQ ID NO:3 (Figure 2A); polynucleotides of 254P1D6B v.2 as encoding SEQ ID NO:5 (Figure 2B) and 254P1D6B v.3 as encoding SEQ ID NO:7 (Figure 2C). The specification fails to provide a nexus between the expression of 254P1D6B (SEQ ID NO:1) in cancerous lung, ovary, prostate, pancreas and breast and the expression of the individual variant sequences. The specification does not provide any objective evidence that the variant sequences can be used as markers of the cancerous state. There is no objective evidence that all the variants possess any property as reported for the 254P1D6B (SEQ ID NO:1) sequence. Further, there are no teachings for how to use the polypeptide of claims 54 and 56 if said peptides do not generate an antibody which binds a polypeptide associated with a cancerous state. There are many examples known in the art of differing expression and function between protein variants. For

instance, Matsushita et al (FEBS Letters, 1999, Vol. 443, pp. 348-352) teach that latrophilins exhibit alternative splicing resulting in latrophilin-1 which is present in brain and endocrine cells, latrophilin-2 which is ubiquitous, and latrophilin-3 which is brain-specific. Singh et al (Glycobiology, 2001, Vol. 11, pp. 587-592) teach that the CD44 splice variant, CD44v, is the major PNA-binding glycoprotein in colon cancer cells in contrast to standard CD44. Zwhalen et al (International Journal of Cancer, 2000, vol. 88, pp. 66-70) teach the expression of p73 splice variants in ovarian adenomas to the exclusion of wild-type p73. These references serve to demonstrate that one of skill in the art cannot anticipate the biological activity or tissue distribution of protein variants based on the biological activity or tissue distribution of the wild-type protein or a single protein isoform. Therefore the specification is lacking a specific, and substantial utility for the variant sequences because the utility as set forth in the specification for SEQ ID NO:1 cannot be translated into the same utility for the variant sequences.

Claims 63, 66 and 72 are drawn to the polynucleotides encoding the polypeptides of SEQ ID NO3, 5 or 7, full complements thereof; and polynucleotides comprising SEQ ID NO:2, 4 and 6. Claims 58 is drawn to a method of generating an immune response in a mammal comprising exposing cells of said mammal to a polypeptide comprising SEQ ID NO:3, 5 or 7 wherein said immune response is the activation of B cell and thus the production of antibodies. All of said claims lack utility because the proteins which are encoded by the nucleic acids and the proteins to which the immune response is directed lack utility for the reasons set forth above.

If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polynucleotide to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed polynucleotide is either present only in cancer tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue. Evidence of a differential expression might serve as a basis for use of the claimed polynucleotide as a diagnostic for a disease. However, in the absence of any disclosed relationship between the claimed polynucleotide or the protein that is encoded thereby and any disease or disorder and the lack of any correlation between the claimed polynucleotide or the encoded protein with any

known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." Brenner, 148 USPQ at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. §101.

The instant situation is directly analogous to that which was addressed in Brenner v. Manson, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

The instant claims are based on protein variants of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the variants of SEQ ID NO:3, 5 and 7 were, as of the filing date, useful for the diagnosis of cancer or the generation of an immune response against a cancerous cell.. Until some actual and specific significance can be attributed to the SEQ ID NO:3, 5 and 7, or the encoding polynucleotides, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Such a use has been determined by the courts to be a utility which, alone, does not support patentability. Since the

instant specification does not disclose a credible "real world" use for the variant proteins of the instant invention, then the claimed invention as disclosed does not meet the requirements of 35 U.S.C. §101 as being useful.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 49, 54, 56-58, 63, 66, 72, 75, 79 and 80 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant argues against the notion that 254P1D6B is solely the SSH DNA and states that the specification as a whole and in context is referring to the collective-related proteins to 254P1D6B. This has been considered but not found persuasive. The specification refers to the SSH protein as the 254P1D6B protein and the variants, and homologs as 254P1D6B-related proteins rather than 254P1D6B protein. There is no evidence to suggest that separate data was obtained for each of SEQ ID NO:3, 5 and 7 for every assay presented in the specification. It is noted that it is unclear if a single 254P1D6B, a combination of 254P1D6B of all of SEQ ID NO:3, 5, 7 or encoding polynucleotide is amplified in Figure 14A.

Applicant argues that the proteins of the invention meet the bar of U.S.C. 101 if they can be used in "any reasonable use". Applicant maintains that the variant proteins, (254P1D6B-related proteins), of the invention are involved in cancers in the same or different tissues thus serving as a family of tumor-associated markers. This has been considered but not found persuasive. The specification fails to teach that SEQ ID NO:3, 5, or 7, per se, are differentially expressed, over expressed, or mis-expressed in any cancer. There are no teachings to specifically correlate any or all of the variant sequences with a particular cancerous tissue.

Applicant argues that the fu length 254P1D6B protein was identified by using the SSH sequence as well as the polynucleotides encoding the variant sequences. This is not persuasive because simple hybridization is not a indication of differential expression, even when the sequences are closely related in structure.

Applicant argues that figures 14-16 provide for strong expression of 254P1D6B in lung and ovarian cancer pools. This is true, however, it is the examiner contention that "254P1D6B" does not represent each or any of the 254P1D6B-realted proteins of SEQ ID NO:3, 5 or 7.

Applicant argues that the expression data provides for a real world use for the 254P1D6B-realted polypeptides of SEQ ID NO:5, 7 and 9. This is not persuasive, because the examiner maintains that there is no assertion that SEQ ID NO:3, 5, and 7 are included together or separately in the expression data presented in the specification and the figures.

All claims are rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A. Canella/
Ph.D., Primary Examiner
Art Unit 1643